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ΤΜΗΜΑ ΕΠΙΣΤΗΜΗΣ ΦΥΣΙΚΗΣ ΑΓΩΓΗΣ ΚΑΙ ΑΘΛΗΤΙΣΜΟΥ

SHORT TERM EFFECTS OF CONVENTIONAL AND ELECTRONIC CIGARETTE SMOKING TO PULMONARY FUNCTION IN PATIENTS WITH DIAGNOSED COPD (CHRONIC OBSTRUCTIVE PULMONARY DISEASE)

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Μεταπτυχιακή Διατριβή που υποβάλλεται στο καθηγητικό σώμα για τη μερική εκπλήρωση των υποχρεώσεων απόκτησης του μεταπτυχιακού τίτλου του Προγράμματος Μεταπτυχιακών Σπουδών «Άσκηση και Υγεία» του Τμήματος Επιστήμης Φυσικής Αγωγής και Αθλητισμού του Πανεπιστημίου Θεσσαλίας.

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ΠΕΡΙΛΗΨΗ

Το ηλεκτρονικό τσιγάρο είναι μια εναλλακτική μορφή καπνίσματος, ένα προϊόν της σύγχρονης τεχνολογίας που αποτελείται από μια επαναφορτιζόμενη μπαταρία, τον ατμοποιητή και τα αναλώσιμα φίλτρα, σε μια συσκευή που μοιάζει με τα συμβατικά τσιγάρα. Η ευρεία κατανάλωση των ηλεκτρονικών τσιγάρων έχει εγείρει το ενδιαφέρον και την ανησυχία της ιατρικής κοινότητας διεθνώς, από τη στιγμή που δεν υπάρχει ικανός αριθμός τεκμηριωμένων ερευνών ως προς τις πιθανές παρενέργειες τους ή οφέλη τους. Η παρούσα μελέτη εξετάζει τις βραχυπρόθεσμες επιπτώσεις του ενεργητικού καπνίσματος συμβατικού και ηλεκτρονικού τσιγάρου σε ασθενείς με διαγνωσμένη Χρόνια Αποφρακτική Πνευμονοπάθεια (ΧΑΠ). Εξετάσθηκαν 16 εθελοντές (8 άνδρες, 8 γυναίκες, όλοι καπνιστές με >25p/y) που υποβλήθηκαν σε τρείς συνεδρίες: μια κατάσταση ελέγχου, μια κατάσταση ενεργητικού καπνίσματος συμβατικού τσιγάρου και μια κατάσταση ενεργητικού καπνίσματος ηλεκτρονικού τσιγάρου. Σπιρομετρικός έλεγχος πραγματοποιήθηκε ακριβώς μετά το κάπνισμα σε κάθε συνεδρία. Επίσης, δεδομένα οξυμετρίας και αερίων αίματος συλλέχθηκαν σε όλες τις συνεδρίες σε τρείς φάσεις (πριν το κάπνισμα, ακριβώς μετά το κάπνισμα, και μια ώρα μετά το κάπνισμα). Τα αποτελέσματα του σπιρομετρικού ελέγχου έδειξαν ότι τα συμβατικά τσιγάρα επηρεάζουν σημαντικά τη λειτουργία του αναπνευστικού, όπως φάνηκε από τις σημαντικές πτώσεις στο FEV1 και στο Δείκτη Tiffneau ($p<0.05$). Αντίθετα, τα ηλεκτρονικά τσιγάρα δεν άλλαξαν σημαντικά τα αποτελέσματα του σπιρομετρικού ελέγχου ($p>0.05$). Τα συμβατικά τσιγάρα επηρέασαν αρνητικά τα PaO2, PaCO2, HCO3, και την οξυμετρία ($p<0.05$). Αντίθετα, τα ηλεκτρονικά τσιγάρα δεν επηρέασαν σημαντικά τα αποτελέσματα των μετρήσεων αυτών ($p>0.05$). Με βάση τα παραπάνω, συμπεραίνεται ότι το κάπνισμα ηλεκτρονικού τσιγάρου δεν επιφέρει σημαντικές

βραχυπρόθεσμες μεταβολές στους δείκτες του σπιρομετρικού ελέγχου, οξυμετρίας και αερίων αίματος σε ασθενείς με διαγνωσμένη ΧΑΠ.

Λέξεις-κλειδιά: ηλεκτρονικά τσιγάρα, κάπνισμα, ΧΑΠ, αναπνευστική λειτουργία, σπιρομέτρηση.

ABSTRACT

Electronic cigarette is an alternative mode of smoking, a product of modern technology that is consisted of a battery powered device that has a simulating role in vaporizing nicotine into inhalable vapour and filters in size and shape similar to conventional cigarette. Its growing popularity starts to alert the medical community worldwide from the moment that there are not sufficient, scientifically documented research results for their possible benefits or hazards on healthy population or among people with chronic diseases. In this randomized crossover trial we attempt to examine the acute effects of conventional and electronic cigarette smoking in 16 patients (8 male, 8 female, all active smokers >25p/y) with diagnosed Chronic Obstructive Pulmonary disease (COPD). They were examined in three sessions, a control condition, a conventional cigarette smoking condition and an electronic cigarette condition. Spirometry measurements were taken immediately after smoking in each condition. Moreover, oxygen saturation and arterial blood gases were measured before, immediately after smoking, and one hour after smoking in each condition. The results from spirometry demonstrated that tobacco cigarettes generated a significant detrimental effect on lung function, evident by the reduction in FEV1 and Tiffneau Index ($p<0.05$). In contrast, e-cigarettes did not produce any statistically significant effects on spirometry results ($p>0.05$). In terms of arterial blood gas analysis, PaO2, PaCO2, HCO3, and oxygen saturation were unfavourably affected by tobacco cigarettes ($p<0.05$). In contrast, e-cigarettes did not produce any statistically significant effects on the results of arterial blood gases ($p>0.05$). Based on the results of this study, it is concluded that acute e-cigarette smoking does not affect lung function (as assessed by spirometry) and arterial blood gases in COPD patients. In contrast,

acute tobacco cigarette smoking undermines lung function and arterial blood gases in these patients.

Keywords: e-cigarettes, smoking, tobacco, COPD, lung function, spirometry.

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1. INTRODUCTION

Cigarette smoking began centuries ago and currently ~20% of the world's adult population smokes cigarettes. Smokers consumed nearly 5.9 trillion cigarettes in 2009, representing a 13% increase in consumption compared to 1999 (WHO, 2008b). In terms of cigarette consumption, Greece is the first country among the European countries and third in the world, in both sexes, while it was 6th in the consumption of tobacco worldwide in 2008 (WHO, 2008b). The increased prevalence of smoking is ever increasing, despite its advertised unfavourable health effects. The World Health Organization states that smoking kills one person every six and half seconds somewhere in the world; this is either because of direct smoking or passive smoking (WHO, 2012). According to recent data, smoking is responsible for killing one person out of five people who suffer from cancer or around 1.4 million death cases around the world every year (WHO, 2012).

Given the economic and public health concerns for smoking, smoking cessation is a major concern in order to reduce morbidity and mortality. Behavioural modification, nicotine replacement products (e.g. patches, gums etc), medications (bupropion, varenicline) and lately electronic cigarettes are the means that are usually used. The electronic cigarette (e-cigarette) was introduced in China in 2004, patented by a pharmacist, and then it was widespread worldwide. Its popularity has increased over the last years based on the advertised claim that it can be used as an effective means of reducing or stopping smoking, a smoke-free method in public places, and also as a cheaper way of smoking (Ayers et al., 2011). However, only limited data are available on e-cigarettes. On their website, the U.S. FDA states that "E-cigarettes may contain ingredients that are known to be toxic to humans, and may contain other ingredients that may not be safe". They also suggest that because their manufacturers are not required to submit clinical study data to them, the public has no way of

knowing " whether e-cigarettes are safe for their intended use, what types or concentrations of potentially harmful chemicals are found in these products, or how much nicotine they are inhaling when they use these products." The FDA is also concerned that the marketing effects of e-cigarettes may increase addiction to nicotine, especially in young people, encouraging them to experiment with real tobacco products. Similar statements have been made from WHO (WHO study group on tobacco product regulation, 2009).

Lung function tests on patients with chronic obstructive pulmonary disease (COPD) using e-cigarettes lack at this moment. At present, most clinicians are sceptical about their use and they don't recommend e-cigarettes as a means of stopping cigarette smoking. Active smoking is a well-known process that gradually produces a deterioration of lung function (Flouris & Koutedakis 2011) but there is no such evidence concerning the e-cigarette. No matter if e-cigarette is a pioneer product, there are limited data concerning its efficiency but most important, of their safety (Flouris & Oikonomou, 2010).

1.1. Aim of the study

In this study our aim was to analyse the effects of conventional and e-cigarette consumption based on basic parameters such as spirometry and arterial blood gas analysis. For this reason we recruited COPD patients with different grade of severity of disease.

The expected impact of this work is to report if there is any clinical significance of our results, in order to help the healthcare community to provide recommendations to COPD patients regarding the use of e-cigarettes.

2. LITERATURE REVIEW

2.1. History of tobacco smoking

Tobacco, a native plant of Americas was first discovered 18.000 years ago when migrant Asiatic people crossed the Bering Strait and spread across the continents known today as the Americas where tobacco is native (Gilman & Xun, 2004). Tobacco is related to garden vegetables belonging to the family plant of Solanaceae; the genus Nicotiana Contaius with about 100 species, only two of which have been extensively cultivated Nicotiana Tabacum (being the predominant mostly used crop tobacco) and Nicotiana Rustica.

Tobacco use dates back as early as 5.000 – 3.000 BC, used by Indians of North America in the region Andes (Gilman & Xun, 2004). It was used for ritual ceremonies and smoke was believed to carry the prayers to gods. Beside the ritual practices, it was believed to be a cure-all, e.g. to dress wounds and as an analgesic. Tobacco chewing was probably the first way that tobacco was consumed. In that way it was believed to relieve toothache. Anthropologists speculated that snuffling – taking powdered tobacco through the nose – probably predated smoking. Snuffing Y shaped tubes are among the earliest tobacco artefacts discovered in the Americas (Gilman & Xun, 2004).

The name tobacco was originally applied to the plant in error. In fact this term referred to the cane pipe, called tobacco or tavaco, with two branches for the nostrils, which has been used by the native Americas for sniffing tobacco smoke (Gately, 2001). Smoking tobacco by the natives was made able by wrapping leaf in corn husk to produce the forerunner of cigarette. Soon after the first trip of Colombus, it didn't take long for tobacco to be criticized on a Christianity basis. Hispaniola's military governor, Gonzalo Fernadez de Oviedo, wrote of the indigenous people's evil customs emphasizing on "one that is especially harmful: the ingestion of a certain kind of smoke, they call tobacco, in order to produce a

state of stupor". He concluded that its use has a harmful effect appears to be spiritual, as the productive soul is deadened by the product's intoxicating quality (Gately, 2001).

European Christians soon observed tobacco in native ritual that looked absolutely satanic "an active tool of the Antichrist" as well as in individual instances by shamans who seemed to use it as a "medium for communication with the devil himself" (Gately, 2001). Early European practitioners noticed its power and it's addictive properties. Colombus is quoted having said "it was not within their power to refrain" from smoking having become accustomed to it (Parker & Pope, 2001).

Through the native Indians and based on their assumption of its therapeutic effect, as an analgesic and local antiseptic (Gately, 2001), the first seeds were taken to Europe (Spain) in 1559 by Hernadez Bancolo of Toledo. Ambassador of France in Portugal Jean Nicot de Villemain (1530-1600) introduced its use in France, as a wonder drug to the French court, and soon by mid 1600 tobacco had been introduced to every major civilized culture around the world through major trade routes to ports and markets (Gately, 2001).

Tobacco got a boost in Europe for its reputed medicinal properties as taught by Jean Nicot who had heard stories of tobacco's curative power and sent seeds to Catherine de Medici (Gately, 2001). Through most known as an appetite suppressant, physicians went so far as to prescribe smoking to prevent the plague (Gately, 2001). Meanwhile, a pamphlet entitled Joyful News of our Newe Founde Worlde published by Spanish doctor Nicolas Monardes praised the tobacco use while underlying that someone should be "careful to refute…the charge that tobacco was the Devil's herb". The pamphlet generated a wave of interest in tobacco across Europe as it was translated into Latin, English, French and Italian (Gately, 2001). Gradually the new habit of smoking tobacco started to be affordable not only by the rich people and became available to the majority of people in Europe (Gilman & Xun, 2004).

Smoking for pleasure received its greatest endorsement from Sir Walter Raleigh who was “a favourite of the queen of England being something of a trendsetter in the fashion – conscious circles of Elizabethan London” (Parker & Pope, 2001). The popularity of tobacco in England prompted the English colonial tobacco industry, which was boosted by John Rolfe’s move in Jamestown to acquire the finer Nicotiana Tobaccum (to replace the more bitter rustica) allowing the first shipment of tobacco to England by 1613 (Parker & Pope, 2001).

The English developed a preference for the pipe, based on their interactions with North American Indians, while the Spanish preferred the cigar a closer relative to the smoking encountered on their exploration in the New World (Parker & Pope, 2001). Sniff was popular in the French court and it soon spread into the country as tobacco prices came down; again also thanks to big tobacco ventures in the New World. Americans themselves developed a strong preference for chewing tobacco, a habit disdained by Continental visitors but one that remained popular into the 19th century (Parker & Pope, 2001).

Around the world, sailors and global trade disseminated tobacco and smoking habits. Cultivation became widespread not only in America, but across the African and Asian continents as well. Its use not only in the Ottoman Empire but also in India, Africa and Central Asia was widespread with great speed (Parker & Pope, 2001). Even Japan became familiar with the new habit around 1540. Tobacco was instantly popular though, as elsewhere, first in the higher status of Japanese society, where it was favoured by samurai knights who created “ornate silver tobacco pipes” and formed smoking clubs in which to gather and share in the pleasure of tobacco (Parker & Pope, 2001).

Early in the 19th century, while much of Europe was under Napoleonic influence, the French army occupying Spain came into contact with popular Spanish tobacco products including the cigaritos, the Spanish diminiture of cigar which gradually became so popular

becoming cigarette in French, now “the most commonly used French word in the planet” (Gately, 2001). Beside advertisement, two key innovations helped its widespread use during the 19th century. First, in 1839 after an accident with fire near a tobacco storage house it was proven that dried tobacco was much milder and more flavourful (Parker & Pope, 2001). The second innovation was when Virginian James Bonsack patented a machine to manufacture cigarettes and Bull Durcham took a gamble on the machine as tobacco’s future. When the machine begun producing 200 cigarettes a minute – as many as 40 human employees rolling by hand – the future of the cigarette was, indeed, solidified (Gately, 2001).

Due to the widespread popularity of smoking among the European societies and even worldwide, soon appeared legislations against it (Lader & Henningfield, 1985). One of the earliest bans was a 1575 regulation by the Mexican church which forbade smoking in churches in Mexico and at the Spanish colonies in the Caribbean (Lader & Henningfield, 1985). In England, in 1604 king James I of England regulated the Counterblaste to Tobacco that had the effect of taxes on tobacco trade (Lader & Malcolm 1985). At East, Sultan Murad IV prohibited smoking in the entire Ottoman Empire in 1633. Pope Urban VII and VIII prohibited smoking in the church at 1590 and 1633 respectively (Lader & Malcolm 1985). In central Europe, banning of smoking appeared first in the Bavarian region of Germany and certain parts of Austria in the late 17th century (Lader & Malcolm 1985).

The first attempt in modern history to restrict smoking was held by the Nazi regime in any public service of the country. Under the instructions of Karl Astel’s Institute for Tobacco Hazards Research, this ban was announced in 1941 under orders from Adolf Hitler (Proctor, 2001). Major anti-tobacco campaigns were widely broadcasted by the Nazis until the fall of the regime (Proctor, 1996). After the 1950’s, evidence of the correlation of smoking with several diseases (especially lung cancer) started accumulating. Individuals started to sue the

companies by the mid 1950's (MSA Agreement). The accusations were mostly about negligent manufacture (Proctor, 1996).

Different policies were enforced around the world in the latter part of the 20th century. Ban of smoking in USA started from 1975, in the US state of Minnesota, prohibiting smoking in public spaces. Gradually other states including Colorado and California followed Minnesota's example ((King & Siegel, 2001; www.no-smoke.org). In November 1988, the four largest United States tobacco companies and the attorney general of 46 states signed the Tobacco Master Settlement Agreement. The states settled with the companies for recovery of their tobacco-related health care costs and also exempted the companies from private tort liability regarding harm caused by tobacco use. Furthermore, this agreement ensured that the companies will invest large amounts of funds for advertising the health risks of smoking, that they will collaborate towards reducing smoking initiation by youth, and that they will fund the creation of an antismoking institute (King & Siegel, 2001).

In Peru it is illegal to smoke in any public enclosed places and in any public transport vehicles (law 25357) since 1993. By December 2004 there was a smoking ban in schools and workplaces in New Zealand (Smoke free law in New Zealand. moh.govt.nz). In 2004 Ireland became the first country in Europe to ban smoking in all workplaces, including bars and restaurants. By 2007, smoking was banned in all public places in most European countries and Turkey took such measures in 2008.

Despite these measures as well as the well-known dangers of smoking, tobacco consumption is steady rising (WHO, 2008b). Nearly 20% of the world's adult population smokes cigarettes. Smokers consumed nearly 5.9 trillion cigarettes in 2009, representing a 13% increase in consumption during the past decade (WHO, 2008b; www.tobaccoatlas.org). Greece is the first country among the European countries and third in the whole world, in

both sexes, while it was 6th in the consumption of tobacco worldwide in 2008 (WHO, 2008b).

2.2. Health hazards of cigarette smoking

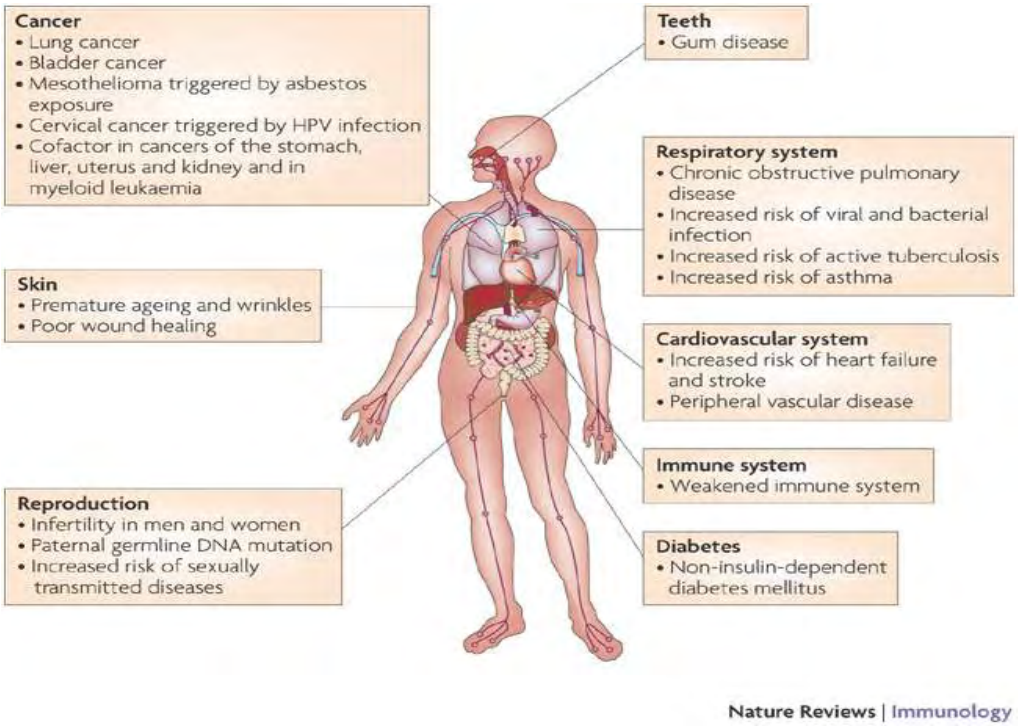
The Journal of the American Medical Association published the landmark 1950 studies of Ernest Wynder (Wynder & Graham, 1950) and Martin Levin (Levin et al., 1950) that showed a statistical correlation between incidents of lung cancer and heavy smokers. The British Medical Journal followed (Doll & Hill, 1950), and the two journals became homes to many studies to be released over the following decades demonstrating statistical reason of concern. Negative health effects had long been suspected to be related to some part of the process of smoking, but the deep inhalation of smoke by cigarette smokers was proven to be especially harmful, and such studies became the catalyst for countless additional examinations into the ancient pleasure of tobacco.

Cigarette consumption historically has been highest in high income countries, but because of targeted marketing, increased social acceptability, continued economic development, and population increases, consumption is expected to increase in low and middle income countries (WHO, 2012). Cigarette consumption in Western Europe dropped by 26% between 1990 and 2009 but increased in Middle East and Africa by 57% during the same period. This change has occurred as people in high-income countries increasingly understand the dangers of smoking and governments continue to implement tobacco control policy and legislation. Globally the increase in cigarette consumption in low- and middle-income countries is significantly enough to offset the decrease in high-income countries (WHO, 2012). Another factor related to global smoking prevalence is the population growth. China is a typical example. Chinese men smoke a third of the world's cigarettes. As Chinese women smokers also increase in numbers, global consumption of cigarettes will skyrocket

and the country's economy and healthcare system will be overwhelmed, as this has happened in other countries in the past (WHO, 2012).

Cigarette smoking is the number one cause of preventable disease and death worldwide (WHO, 2012; www.lung.org). Smoking harms nearly every organ in the body, and it is a main cause of lung cancer and COPD. It is also a cause of coronary heart disease, stroke and a host of other cancers and diseases (US Department of Health and Human Services, 2004), as indicated in figure 1. There are some interesting facts concerning smoking. Cigarette smoke contains over 4.800 chemicals, 69 which are known to cause cancer. Smoking is directly responsible for approximately 90% of lung cancer deaths and approximately 80-90% of chronic obstructive pulmonary disease (COPD; emphysema and chronic bronchitis) deaths (Centers for Disease Control and Prevention, 2004). Among current smokers, chronic lung disease accounts for 73% of smoking-related conditions (Centers for Disease Control and Prevention, 2003).

Figure 1. Health effects of tobacco smoking.



2.3. Smoking Rates among Adults & Youth

In 2009, an estimated 46.6 million or 20.6% of adults (aged 18+) were current smokers (Centers for Disease Control and Prevention, 2009). Men tend to smoke more than women, but their difference starts to decrease. Smoking in pregnancy accounts for an estimated 20-30% of low birth weight babies, up to 14% of preterm deliveries, and 10% of all infant deaths. Even apparently healthy, full term babies of smokers have been found to be born with narrowed airways and reduced lung function (US Department of Health and Human Services, 2001). Moreover, smoking is a major cause of premature death worldwide (WHO, 2011; Jha, 2009).

Passive smoking refers to the smoke that non-smokers are breathing in from the smokers. People who spend time around smokers are breathing in the smoke either from the burning end of the active smoker's cigarette or the smoke exhaled by the active smoker. This is called involuntary or secondary smoking. Exposure to second hand smoke can lead to very serious health problems, such as respiratory diseases, heart disease, lung cancer and even dementia (Chen et al., 2012). Passive smoking is considered a preventable cause of death that has killed thousands of people exposed to cigarette smoke in homes, workplaces and/ or in public (Chen et al., 2012).

When a cigarette is smoked about half of the smoke is inhaled/exhaled (mainstream smoke) by the smoker and the other half floats around in the air (sidestream smoke). The combination of mainstream and sidestream smoke makes up second hand smoke also known as environmental tobacco smoke. When nonsmokers are exposed to second hand smoke, they inhale many of the same cancer-causing chemicals that smokers inhale.

Both sidestream and mainstream smoke are dangerous to nonsmokers. For example, because sidestream smoke is generated at lower temperatures and under different conditions than mainstream smoke, it contains higher concentrations of many of the toxins found in

cigarette smoke. There is no risk free level of exposure to second hand smoke; even small amounts of second hand smoke exposure can be harmful to people's health. The World Health Organization states that smoking kills one person every six and half seconds somewhere in the world; this is either because of direct smoking or passive smoking (WHO, 2012). According to recent data, smoking is responsible for killing one person out of five people who suffer from cancer or around 1.4 million death cases around the world every year (WHO, 2012).

2.4. Active smoking and lung function

Damage to the respiratory system from cigarette smoking is slow, progressive, and deadly. A healthy respiratory system is continuously cleansed. The mucus produced by the respiratory tubules traps dirt and disease-causing organisms, which cilia sweep toward the mouth, where it can be eliminated. Smoking greatly impairs this housekeeping. With the very first inhalation of smoke, the beating of the cilia slows. With time, the cilia become paralyzed and, eventually, disappear altogether (U.S Department of Health and Human Services, 2010). The loss of cilia leads to the development of smoker's cough. The cilia no longer effectively remove mucus, so the individual must cough it up. To make matters worse, excess mucus is produced and accumulates, clogging the air passageways. Pathogenic organisms that are normally removed now have easier access to the respiratory surfaces and the resulting lung congestion favours their growth (U.S Department of Health and Human Services, 2010).

This above-mentioned process causes the development of COPD, an obstructive lung disease in which chronic incompletely reversible airflow limit exists (U.S Department of Health and Human Services, 2010). This airflow limitation is due to breakdown of lung tissue (known as pulmonary emphysema) and small airway disease (known as obstructive bronchiolitis or bronchitis depending the size of the small airways). It develops secondary to

a more pronounced and chronic inflammatory response to inhaled irritants. The most important processes causing lung damage is the oxidative stress produced by the high concentrations of free radicals in tobacco smoke and cytokine release due to inflammation as the body responds to irritant particles such as tobacco smoke in the airway (Flouris et al., 2010). Both of them lead to impaired activity of antiprotease enzymes such as alpha 1-antitrypsin, allowing protease enzymes to damage the lung (Flouris et al., 2010).

Chronic inflammation plays a major role in COPD pathophysiology. Smoking and other airway irritants cause neutrophils, T-lymphocytes, and other inflammatory cells to accumulate in the airways. Once activated, they trigger an inflammatory response in which an influx of molecules, known as inflammatory mediators, navigates to the site in an attempt to destroy and remove inhaled foreign debris (Flouris et al., 2010).

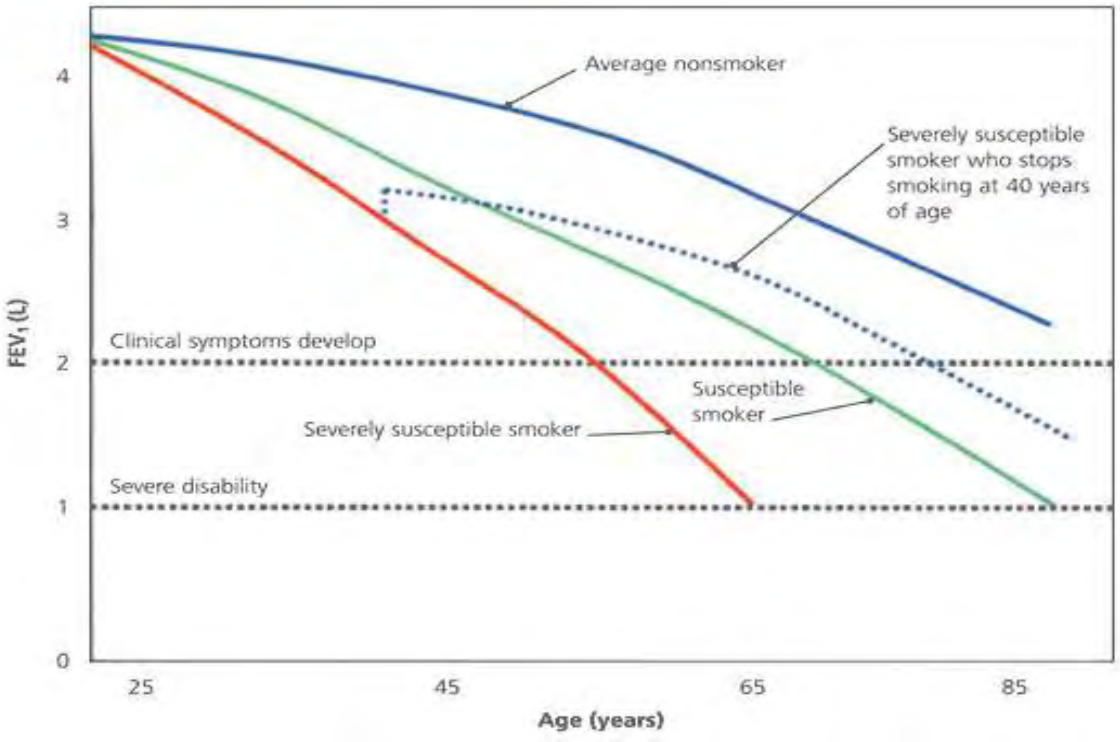
Under normal circumstances, the inflammatory response is useful and leads to healing. In fact, without it, the body would never recover from injury. In COPD, repeated exposure to airway irritants perpetuates an ongoing inflammatory response that never seems to cease. Over time, this process causes structural and physiological lung changes that get progressively worse. As inflammation continues, the airways constrict, becoming excessively narrow and swollen. This leads to excess mucus production and poorly functioning cilia, a combination that makes airway clearance especially difficult. When people with COPD can't clear their secretions, they develop the hallmark symptoms of COPD, including a chronic, productive cough, wheezing and dyspnoea. Finally, the build-up of mucus attracts a host of bacteria that thrive and multiply in the warm, moist environment of the airway and lungs. The end result is further inflammation and bacterial lung infection, a common cause of COPD exacerbation (U.S Department of Health and Human Services, 2010).

Airflow obstruction is defined as a reduced post-bronchodilator FEV1/FVC ratio (where FEV1 is forced expiratory volume in 1 second and FVC is forced vital capacity), such

that FEV1/FVC is less than 0.7 (U.S Department of Health and Human Services, 2010). If FEV1 is 80% or more of predicted normal, a diagnosis of COPD should only be made in the presence of respiratory symptoms, e.g. breathlessness or cough. Patients with COPD may present with loss of lung function beyond normal age-related decreases. Clinical disease develops fairly late in the disease course, after lung function drops below threshold values.

After 25 years of age, a nonsmoking adult's FEV1 decreases by an average of 20 to 40 ml per year (figure 2). In some smokers, FEV1 decreases by two to five times this amount, making them particularly susceptible to COPD (Barnes, 2000). Smoking cessation may cause slight initial improvement in FEV1 (approximately 50 mL in the first year). More importantly, smoking cessation can give a former smoker the same average ongoing loss of lung function as a never-smoker.

Figure 2. The progressive loss of lung function in a variety of settings.



Patients with COPD usually have a smoking history of at least 20 pack-years. Wheezing and dyspnea on exertion generally occur when the FEV1 is less than 50% of the

predicted value, and significant physical disability usually occurs when the FEV1 is less than 35-40% of the predicted value (Doherty, 2002; Mannino 2002). Patients who started smoking in their 20s and have already sustained appreciable FEV1 loss by their 40s are likely to develop significant COPD if they continue to smoke. Those in their mid-40s who have normal FEV1 values, however, probably will not develop symptomatic disease.

The GOLD guidelines (Global Initiative for Obstructive Lung Disease, 2005; American Thoracic Society, 1995) characterize the severity of COPD according to clinical and spirometric measures. Key spirometric measures may be obtained with a portable office spirometer and should include FVC and FEV1. Patients with COPD typically present with obstructive airflow. According to the GOLD criteria, a FEV1/FVC ratio of less than 70% in a patient with a post bronchodilator FEV1 of less than 80% of the predicted value is diagnostic for COPD (Global Initiative for Obstructive Lung Disease, 2005; American Thoracic Society, 1995). Severity is further stratified based on symptoms and FEV1 values. A patient with severe disease has a FEV1 of less than 50% of the predicted value; values below 30% of the predicted value represent very severe disease (Global Initiative for Obstructive Lung Disease, 2005; American Thoracic Society, 1995). Although some experts have proposed periodic FEV1 testing for high-risk patients older than 45 years to facilitate risk factor reduction counselling, no evidence exists to support this recommendation (Global Initiative for Obstructive Lung Disease, 2005; American Thoracic Society, 1995).

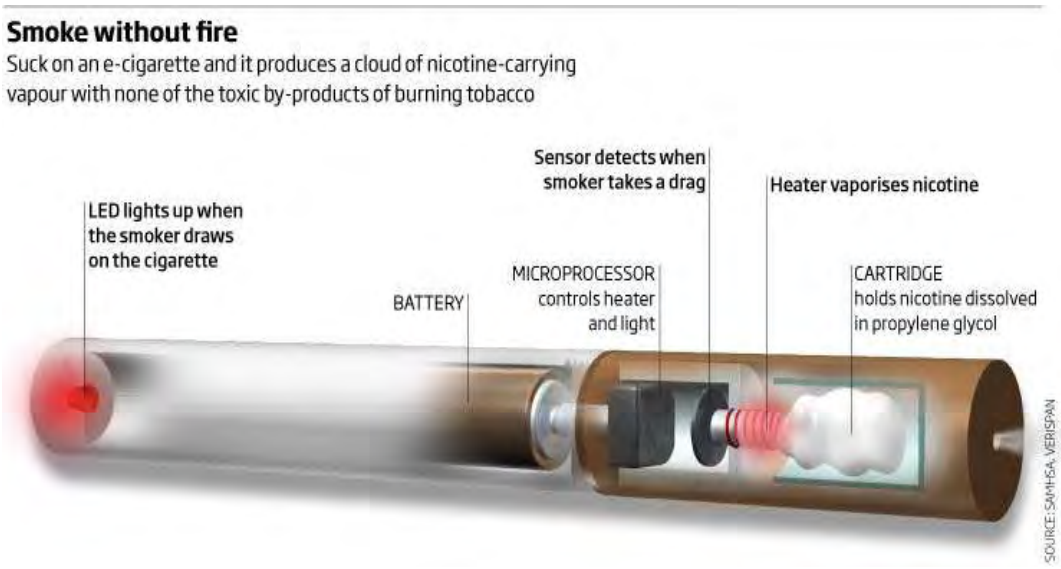
2.5. The introduction of the electronic cigarette

As discussed above, smoking has been an economic and public health issue for many years. Thus, smoking cessation was and certainly is a major issue in order to reduce morbidity and mortality. Behavioural modification, nicotine replacement products (e.g. patches, gums etc),

medications (bupropion, varenicline) and lately electronic cigarettes are the means that are usually used.

The official terminology used to describe the electronic cigarettes is electronic nicotine delivery systems (WHO, 2010). It was introduced in China in 2004, patented from a pharmacist, and then it was widespread worldwide. Its popularity has increased over the last years based on the facts that it can be used as an effective means of reducing or stopping smoking, a smoke-free method in public places, and also as a cheaper way of smoking (Ayers et al., 2011). Electronic cigarettes (e-cigarettes) can be purchased on the internet or through retail venues. Although manual systems also exist, the most popular form is the automatic type. Different brands are available that have different concentration of nicotine, as well as flavours. Most e-cigarette devices are composed of four parts (figure 3): 1) the mouthpiece (or cartridge), 2) the atomizer chamber and heating coil, 3) the battery, and 4) the LED light cover.

Figure 3. Components of most e-cigarette devices.



The mouthpiece is a disposable and opens at each end, contains the liquid that will be vaporized. This liquid is made of nicotine, propylene glycol, flavourings and chemical substances (e.g. rimonabant). This liquid is vaporized by heating, which is inhaled. Below the cartridge is a lithium ion battery and a chip controller with an operating mode sensor and a LED sensor that lights up with a puff. Every e-cigarette includes a rechargeable battery, a battery charger, and a choice of flavour. The cost of the device is about 50 euros or above and each refill costs about 7 euros. Automatic style requires only puffing or taking a drag to activate the atomizer. The e-liquid in the filter heats up to produce the vapour. The concentration of nicotine varies from 0 to 40 mg.

The original intent of an e-cigarette was to imitate the nicotine delivery system of a conventional cigarette without the harmful effects of tobacco smoke combustion (Kuschner et al., 2011). The e-cigarette is advertised to look and taste similar to a real cigarette and to give a nicotine fix. When the button is clicked on the e-cigarette, the liquid nicotine, flavours, and chemicals present in the plastic tube heat up and an atomizer (aerosol) turns into a vapour that is puffed or inhaled and enters into the airway, which is rapidly absorbed into the systemic circulation, giving a dose of nicotine in the brain (http://uspharmacist.com/).

A dispute has been raised over the safety of the chemical components of the e-cigarettes. Data are available about the effects of nicotine so the major interest was focused on the effect of propylene glycol. Also called 1,2 propanediol, it is an organic compound with formula C3H8O2, a colorless, nearly odorless, clear, viscous liquid. It is found in personal care products that act as a penetration enhancer that keeps products from melting in heat and or freezing when it is cold. It is found in items such as shampoo, soap, toothpaste, deodorant, nail polish. According to several sources, it has been linked to cancer, developmental/reproductive issues, allergy and immunotoxicity, neurotoxicity, endocrine disruption and multiorgan toxicity (Choi & Schmidbauer, 2010; www.evg.org).

In the body under conditions of normal low exposure, propylene glycol is quickly metabolized and eliminated. Its metabolic pathway is comparable to that of sugar; it is rapidly converted to lactic acid which is discarded by the body via the urine. Several countries and official institutions have investigated these issues. In the U.S., FDA analysis over nicotine and propylene glycol has showed that PG levels were "generally recognized as safe" provided that their concentration was less than 2% (accessdata.fda.gov). Nicotine release by the e-cigarettes in some specimens was not uniformly released and also the percentage of concentration of nicotine in its liquid was not accurate. Other metabolites such as acetaldehyde, acrolein, polycyclic hydrocarbons and even diethylene glycol were accused of being harmful in the use of e-cigarettes (Westenberger, 2009).

An important issue to be concerned is the rapid growth of the e-cigarette industry and their enormous profits (Pauly & Li, 2007). Smart advertisement campaigns have played a key role to this growth. This industry only in US is expected to double its revenue over last year reaching to a profit of 1 billion dollars, burning away the gap with the traditional cigarette industry (forbes.com). E-cigarette companies take advantage of the lack of law and regulations, as in US that it's free for them to advertise their products on television and give out free samples. Even though there is not enough evidence for their efficiency and safety their use keeps rising (Flouris & Oikonomou, 2010).

E-cigarettes were proposed as a replacement mean or a cessation aid for quitting traditional smoking. As that there was not enough scientific evidence about their safety, WHO asked the manufacturers not to promote them as a therapeutic aid (WHO study group on tobacco product regulation, 2009). In many countries the e-cigarette lacks important regulatory factors, such as health warnings, proper labeling, clear instructions on how to use them, and safe disposal methods (Bullen et al., 2010). There is a big controversy among different studies worldwide about their advantages and disadvantages. During an online

survey conducted in 2010, researchers polled visitors of websites and discussion forums dedicated to the use of e-cigarette and smoking cessation. Of the 3.587 participants, 70% were former smokers, 61% were men, and the median age was 41 years. On average, participants used the e-cigarette for approximately 3 months, drew 120 puffs/day, and used 5 cartridges/day. Almost all of them used cartridges that contained nicotine. A total of 96% stated that the e-cigarette helped them quit smoking, while 92% said that it made them smoke less. A majority of the participants said the e-cigarette helped them fight cravings, cope with withdrawal symptoms, and avoid relapsing on cigarettes (copd.about.com). In another case study series, the e-cigarette was found to help three study participants who all had a documented history of repeated failed attempts at smoking cessation, using professional smoking cessation assistance methods - quit smoking and remain abstinent for at least 6 months (Caponetto et al, 2011).

Limited data are available on e-cigarettes thus making official organizations being aware of their possible harms. On their website, the FDA states that “E-cigarettes may contain ingredients that are known to be toxic to humans, and may contain other ingredients that may not be safe”. They also suggest that because their manufacturers are not required to submit clinical study data to them, the public has no way of knowing “ whether e-cigarettes are safe for their intended use, what types or concentrations of potentially harmful chemicals are found in these products, or how much nicotine they are inhaling when they use these products.” The FDA is also concerned that the marketing effects of e-cigarettes may increase addiction to nicotine, especially in young people, encouraging them to experiment with real tobacco products. Similar statements have been made from WHO (WHO study group on tobacco product regulation, 2009).

3. METHODOLOGY

3.1. Participants

A total number of 16 volunteers with diagnosed COPD and ≥25 pack/years participated: 8 males; 8 females; age: 65.9±9.4 years; pack years: 65.1±28.2; Fagerstrom scale: 7.5±1.6. Written consent was obtained by all volunteers (see Supplement). No alteration of therapy was made and no change of usual smoking habits. None of the participants used e-cigarettes in the past.

3.2. Experimental design

The study was conducted according to the principles expressed in the Declaration of Helsinki and was approved by the University of Thessaly Ethics Review Board (see Supplement) and the 3rd Pulmonary clinic of General Hospital Sotiria, Athens. Volunteers were examined during three conditions within a time interval of 10 days: a conventional cigarette smoking condition (TOB), an electronic cigarette condition (eCIG), and a control condition (CON). Prior to the start of each condition, participants were asked to abstain from active and passive smoking for at least 12 hours. The subjects' medical history and smoking habits were recorded during their first visit. During the TOB condition, every volunteer was given half an hour in order to smoke 2 cigarettes of their favourite brand (puffs: 23.8±4.0). In the eCIG condition, volunteers were asked to draw a predetermined number of puffs using an e-cigarette (puffs: 6.7±3.0). During the CON condition, all individuals were asked to pretend that they smoke an unlit cigarette of their favourite brand (puffs: 23.8±4.0). Spirometry measurements were taken immediately after smoking in each condition. Moreover, oxygen saturation and arterial blood gases were measured before, immediately after smoking, and one hour after smoking in each condition.

The e-cigarette used during the eCIG condition was the model Giant (Nobacco GP, Greece). Each device was fully charged before the visit and new cartridges were obtained. The e-cigarette liquid used (Nobacco USA, MIX, Nobacco G.P, Greece) had tobacco flavour and the percentage of nicotine contained was 11 mg/ml, matching the average concentration of conventional cigarettes (which usually range between 0-35 mg/ml).

The total number of puffs drawn by an e-cigarette result in significantly lower percentage of nicotine absorption compared to that generated by the same number of puffs from a conventional cigarette (Eissenberg, 2010; Vansickel, et. al; 2010). On this basis we modified the number of puffs for every volunteer during the eCIG condition based on: 1) the tobacco cigarette to e-cigarette absorption ratio, 2) the content of nicotine on their conventional cigarette, 3) the nicotine concentration of e-cigarette liquid and 4) the number of puffs required to consume 1 ml of e-cigarette liquid. Based on the above facts, the e-cigarette puffs equivalent to that of one tobacco cigarette was calculated based on the equation:

$$\text{e-cigarette puffs} = (\text{TOBnic} \times 1{,}5 \times 50) / \text{eCIG NIC}$$

where TOBnic is the tobacco cigarette content (in mg), 1,5 is the average tobacco cigarette / e-cigarette nicotine absorption ratio, 50 is the average number of puffs required to consume 1 ml of liquid, and eCIG NIC is the e-cigarette liquid nicotine content (in mg/ml). The result in each case was multiplied by 2 since that was the number of conventional cigarettes smoked during the TOB condition. The above methodology has been recently published by our group (Flouris et al., 2013).

3.3. Spirometry

Spirometry measurements were taken immediately after smoking in each condition. It was done by the same investigator in the 3rd Pulmonary clinic of General Hospital Sotiria, Athens according to the American Thoracic Society recommendations (American Thoracic Society

1995) using a portable Spirometer (Spirolab II). The parameters that were taken under consideration were: forced vital capacity (FVC), forced expiratory volume in 1 sec (FEV1), Tiffneau Index (FEV1/FVC), peak expiratory flow, as well as forced expiratory flow in the 25%, 50%, and 75% of FVC.

3.4. Arterial blood gases

Arterial blood gases [i.e., partial pressure of oxygen in arterial blood (PaO2, in mmHg), partial pressure of carbon dioxide in arterial blood (PaCO2, in mmHg), pH, and bicarbonate (HCO3, in mEq/L) were measured before, immediately after smoking, and one hour after smoking in each condition. The measurements were taken from brachial artery and the analysis was made immediately. The procedure took place in 3rd Pulmonary Clinic of General Hospital Sotiria, Athens in its examination room after the consent of every patient. Each patient was informed about the procedure and all hygiene and safety regulations were taken in advance. Special attention was given from the moment that this is an interventional procedure, to be made by an experienced physician using a syringe of 30 G or 31 G.

3.5. Blood oxygenation

Arterial oxygen saturation was measured before, immediately after smoking, and one hour after smoking in each condition. The procedure took place in 3rd Pulmonary Clinic of General Hospital Sotiria, Athens in its examination room after the consent of every patient. For the oximetry a Nonin portable oxymeter was used, placed at the index finger of each patient at the time intervals mentioned above. As a non interventional procedure it was easily accepted by all participants.

3.5. Statistical Analysis

Friedman tests followed by post hoc Wilcoxon signed-rank tests were used to assess changes between conditions for the spirometry data (i.e., TOB, eCIG, and CON). These analyses were also used to assess changes over time (i.e., prior to, immediately after, and one hour after smoking) in each condition. The accepted level of significance was $P \leq 0.05$.

4. RESULTS

The results for FVC are illustrated in figure 4. The Friedman test demonstrated a significant effect of condition (i.e., TOB, eCIG, and CON) on FVC ($p=0.02$). Post hoc Wilcoxon signed-rank tests revealed a significant difference between TOB and CON ($p=0.03$). The results for FEV1 are illustrated in figure 5. The Friedman test demonstrated a significant effect of condition on FEV1 ($p<0.001$). Post hoc Wilcoxon signed-rank tests revealed significant differences between TOB and eCIG ($p<0.001$) and between TOB and CON ($p=0.001$). Results for the Tiffneau Index are illustrated in figure 6. The Friedman test demonstrated a significant effect of condition on the Tiffneau Index ($p=0.02$). Post hoc Wilcoxon signed-rank tests revealed significant differences between TOB and eCIG ($p=0.02$) and between TOB and CON ($p=0.004$). The Friedman tests for PEF (figure 7), FEF25 (figure 8), FEF50 (figure 9), and FEF75 (figure 10), haematocrit (figure 11), as well as haemoglobin (figure 12) did not reveal any statistically significant effects of condition ($p>0.05$).

Figure 4. The forced vital capacity (FVC) during the conventional cigarette (TOB), the electronic cigarette (eCIG), and the control (CON) conditions.

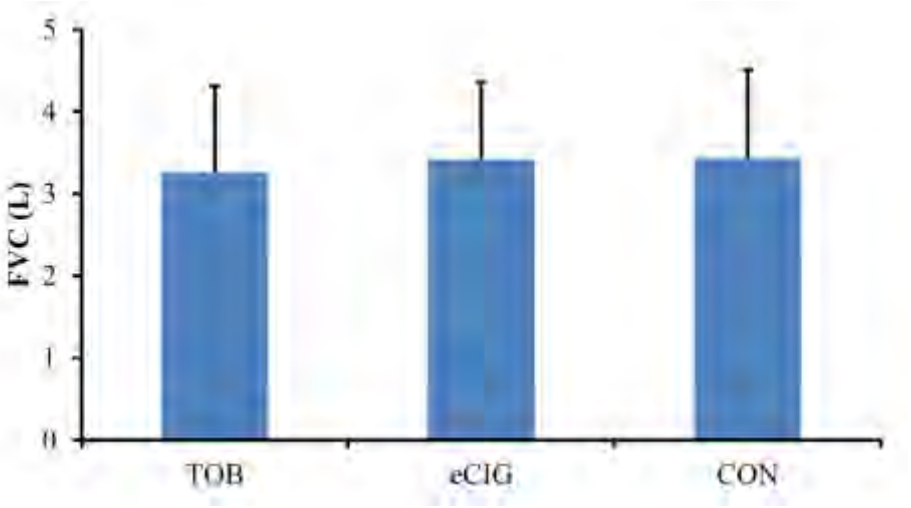


Figure 5. The forced expiratory volume in 1 second (FEV1) during the conventional cigarette (TOB), the electronic cigarette (eCIG), and the control (CON) conditions.

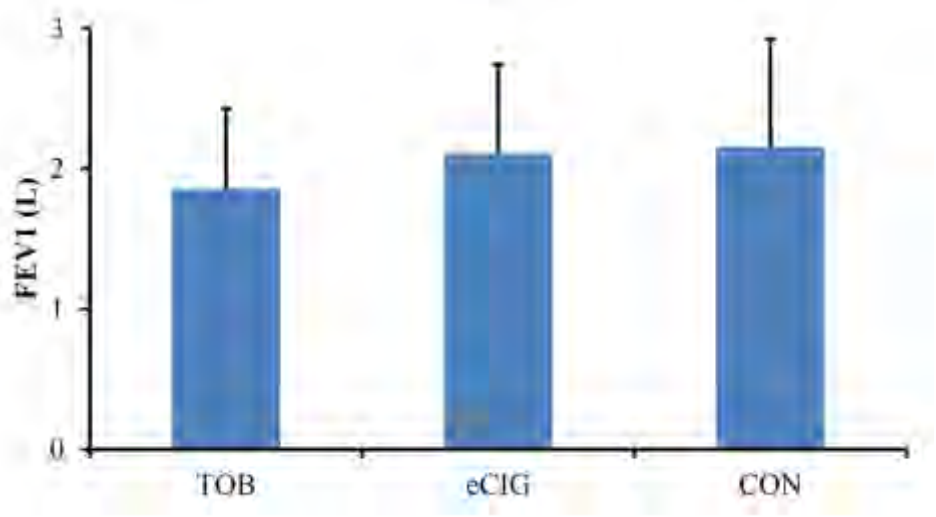


Figure 6. The Tiffneau Index (FEV1/FVC) during the conventional cigarette (TOB), the electronic cigarette (eCIG), and the control (CON) conditions.

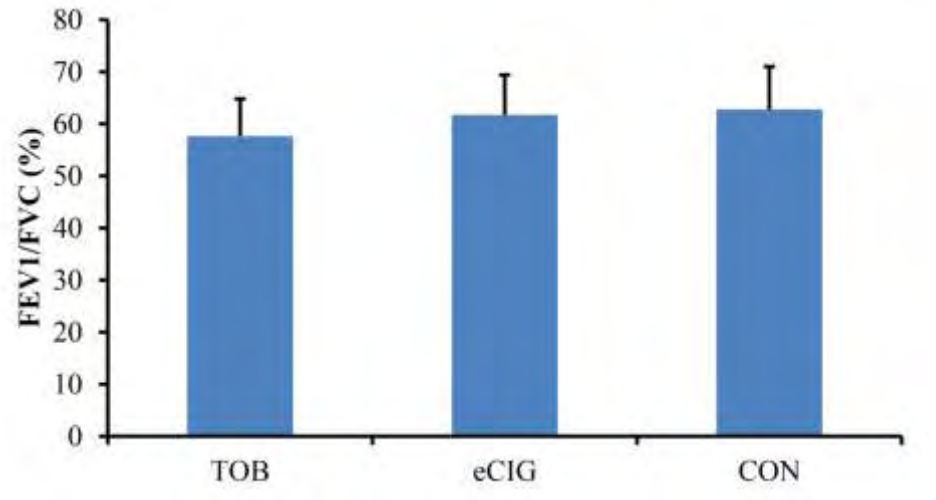


Figure 7. The results for peak expiratory flow (PEF) during the conventional cigarette (TOB), the electronic cigarette (eCIG), and the control (CON) conditions.

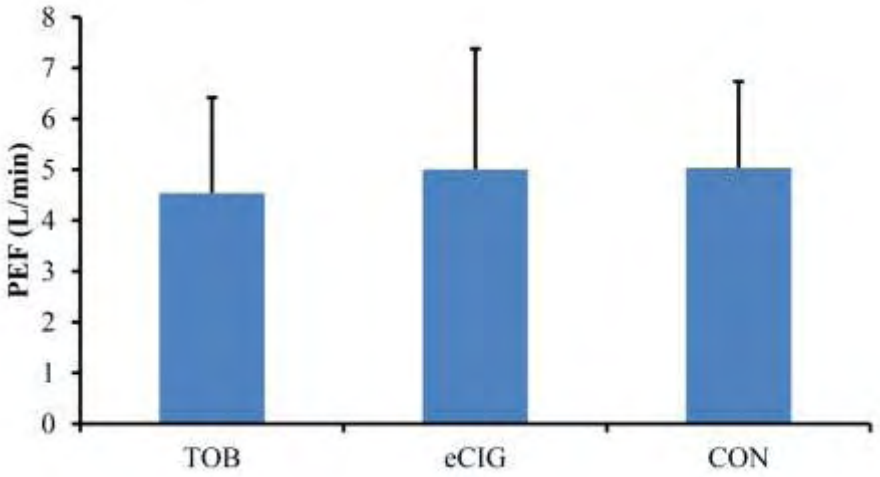


Figure 8. The results for the forced expiratory flow in the 25% of the forced vital capacity (FEF25) during the conventional cigarette (TOB), the electronic cigarette (eCIG), and the control (CON) conditions.

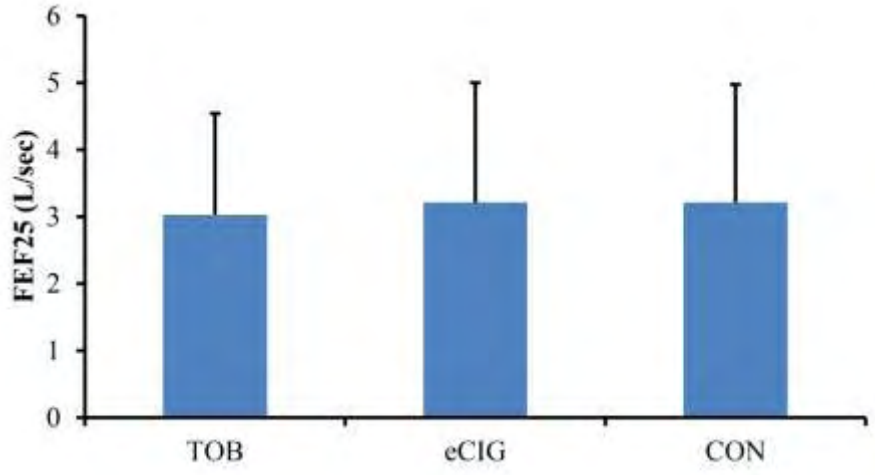


Figure 9. The results for the forced expiratory flow in the 50% of the forced vital capacity (FEF50) during the conventional cigarette (TOB), the electronic cigarette (eCIG), and the control (CON) conditions.

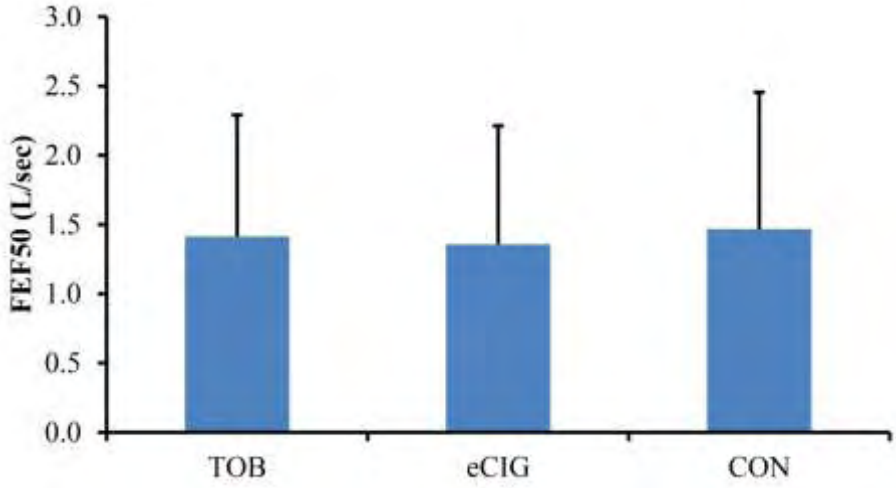


Figure 10. The results for the forced expiratory flow in the 75% of the forced vital capacity (FEF75) during the conventional cigarette (TOB), the electronic cigarette (eCIG), and the control (CON) conditions.

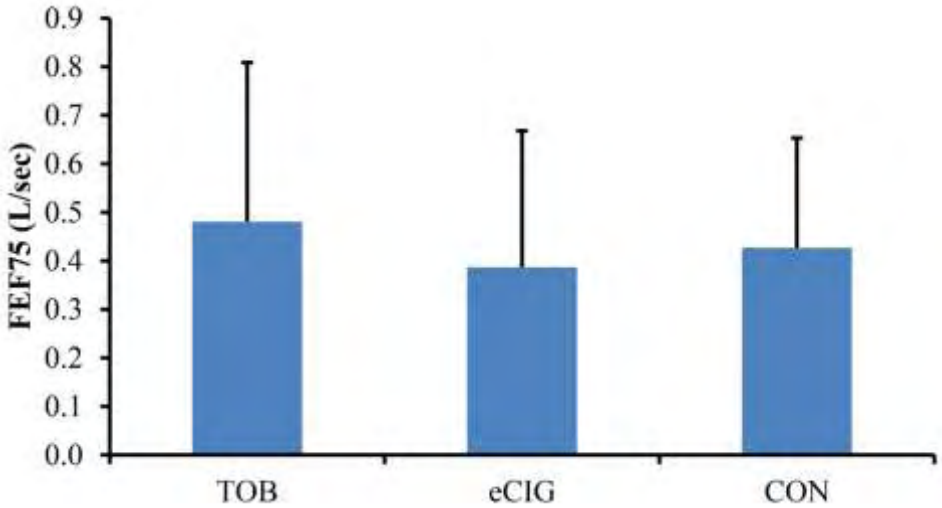


Figure 11. The results for haematocrit during the conventional cigarette (TOB), the electronic cigarette (eCIG), and the control (CON) conditions.

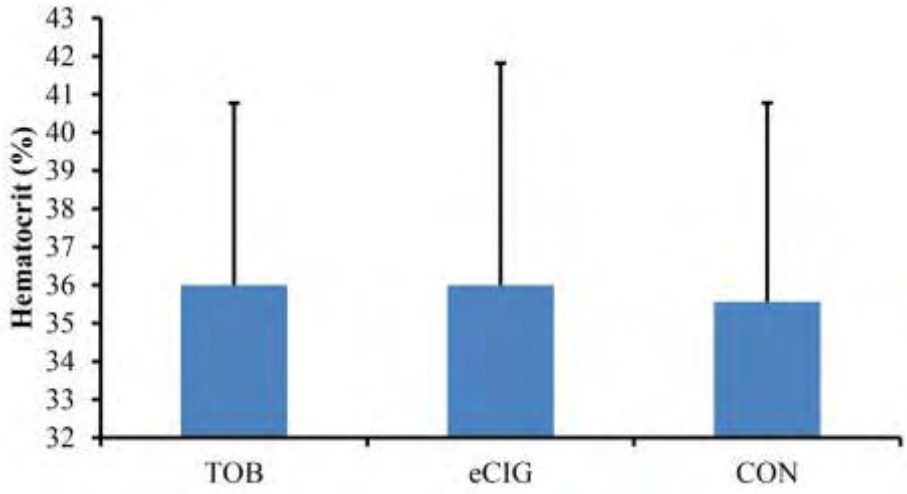
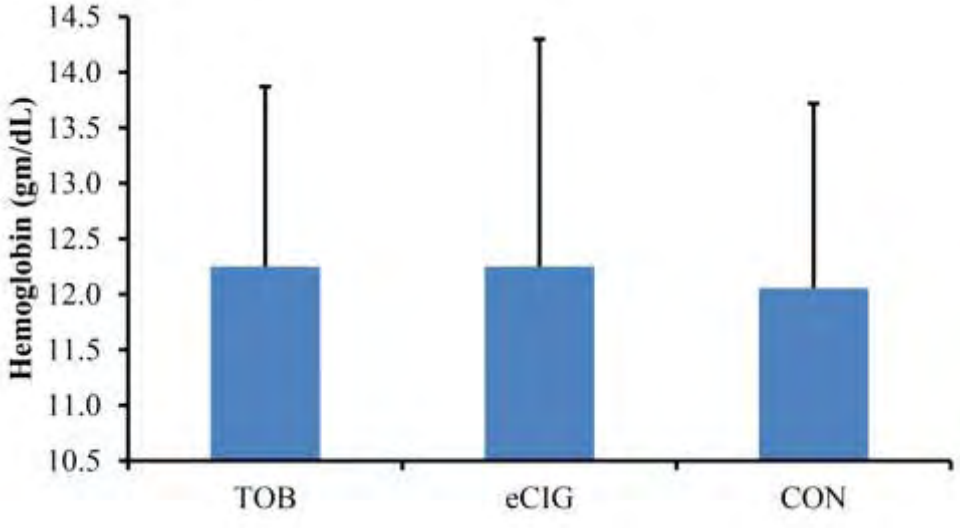


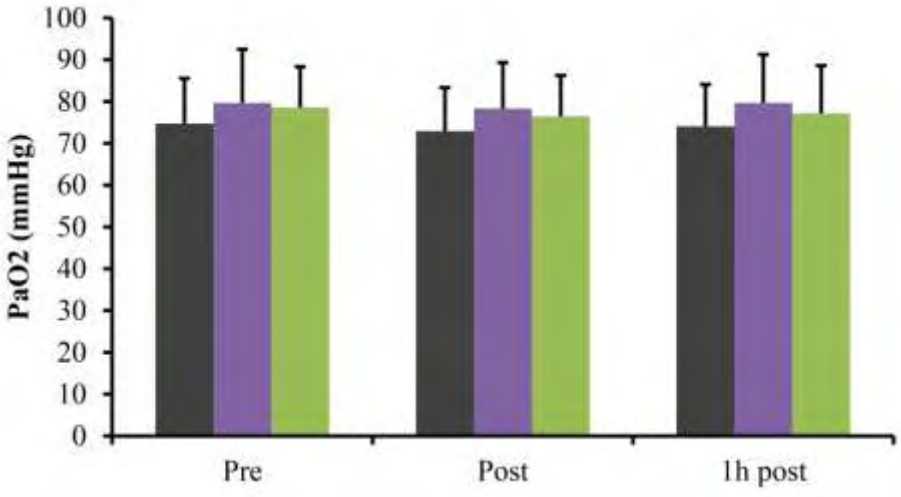
Figure 12. The results for haemoglobin during the conventional cigarette (TOB), the electronic cigarette (eCIG), and the control (CON) conditions.



The results for PaO2 are illustrated in figure 13. Friedman tests demonstrated a significant effect of time (i.e., pre, post, and 1h post) on PaO2 during all conditions ($p<0.05$). Post hoc Wilcoxon signed-rank tests revealed significant differences between pre-post ($p=0.01$) and between post-1h post ($p=0.01$) in the eCIG condition, as well as between pre-

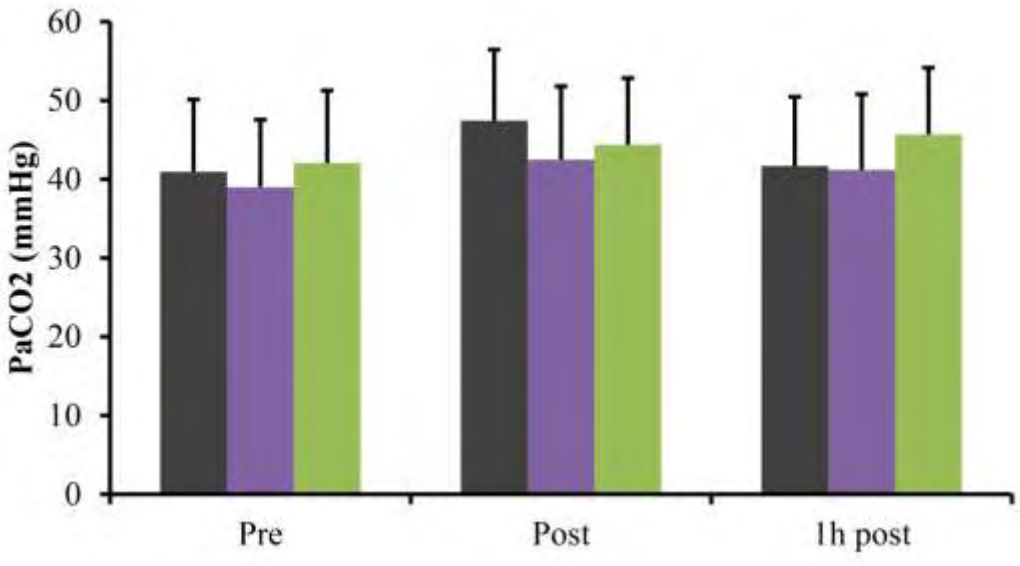
post (p=0.05) in the CON condition. Comparisons within the same time point revealed significant differences between TOB-eCIG and eCIG-CON at baseline, significant differences between TOB-eCIG and TOB-CON immediately after smoking, and a significant difference between TOB-eCIG 1 hour after smoking ($p<0.05$).

Figure 13. The results for the partial pressure of oxygen in arterial blood (PaO2) during the conventional cigarette (TOB; in dark grey), the electronic cigarette (eCIG; in purple), and the control (CON; in light green) conditions.



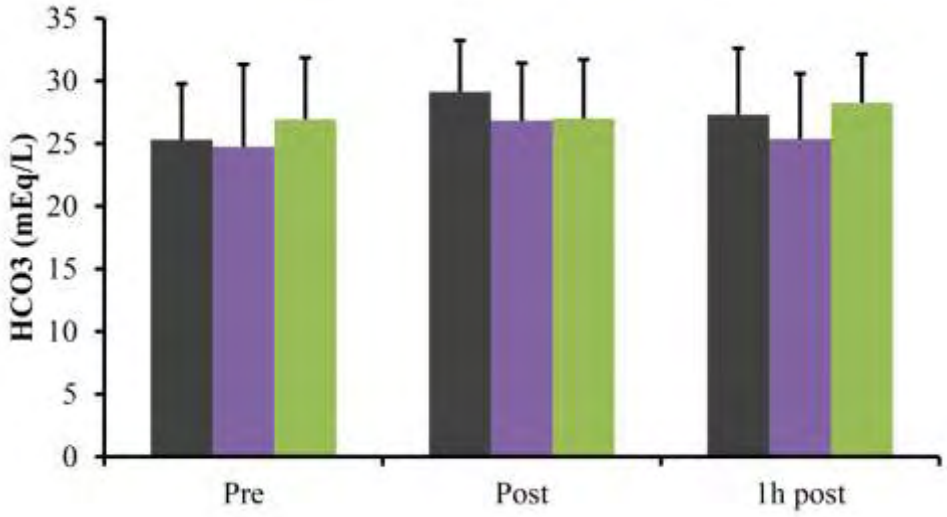
The results for PaCO2 are illustrated in figure 14. Friedman tests demonstrated a significant effect of time (i.e., pre, post, and 1h post) on PaO2 during the TOB condition ($p<0.001$). Post hoc Wilcoxon signed-rank tests revealed significant differences between pre-post (p=0.001) and between post-1h post (p=0.001) in the TOB condition. Comparisons within the same time point revealed a significant difference between TOB-eCIG immediately after smoking, and significant differences between TOB-CON and eCIG-CON 1 hour after smoking ($p<0.05$).

Figure 14. The results for the partial pressure of carbon dioxide in arterial blood (PaCO2) during the conventional cigarette (TOB; in dark grey), the electronic cigarette (eCIG; in purple), and the control (CON; in light green) conditions.



The results for the HCO3 are illustrated in figure 15. Friedman tests demonstrated a significant effect of time (i.e., pre, post, and 1h post) on HCO3 during the TOB condition ($p=0.04$). Post hoc Wilcoxon signed-rank tests revealed significant differences between pre-post ($p=0.001$) and between post-1h post ($p=0.001$) in the TOB condition. Comparisons within the same time point revealed a significant difference between TOB-eCIG immediately after smoking, and a significant difference between eCIG-CON 1 hour after smoking ($p<0.05$).

Figure 15. The results for the bicarbonate (HCO3) during the conventional cigarette (TOB; in dark grey), the electronic cigarette (eCIG; in purple), and the control (CON; in light green) conditions.



The results for pH are illustrated in figure 16. Friedman tests demonstrated no significant effect of time (i.e., pre, post, and 1h post) on pH in any of the conditions ($p>0.05$). Post hoc Wilcoxon comparisons within the same time point revealed significant differences between TOB-eCIG and between TOB-CON 1 hour after smoking ($p<0.05$). The results for oxygen saturation are illustrated in figure 17. Friedman tests demonstrated no significant effect of time (i.e., pre, post, and 1h post) on oxygen saturation in any of the conditions ($p>0.05$). Post hoc Wilcoxon comparisons within the same time point revealed a significant difference between TOB-eCIG at baseline, as well as significant differences between TOB-eCIG and TOB-CON immediately after smoking ($p<0.05$).

Figure 16. The results for pH during the conventional cigarette (TOB; in dark grey), the electronic cigarette (eCIG; in purple), and the control (CON; in light green) conditions.

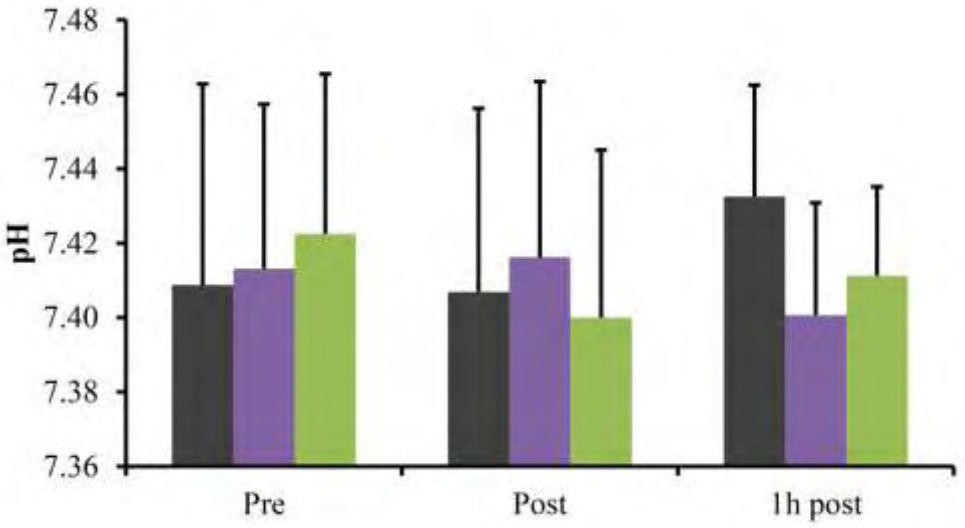
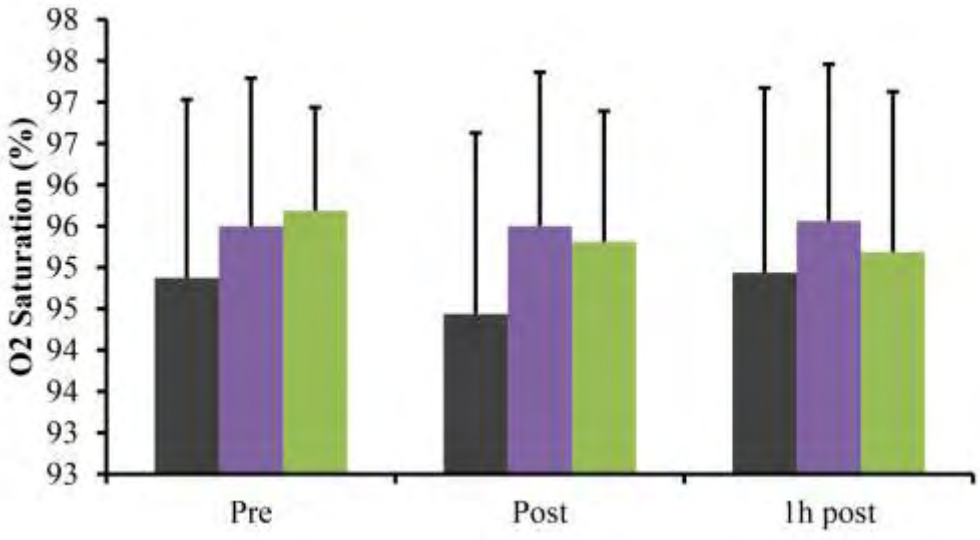


Figure 17. The results for the oxygen saturation during the conventional cigarette (TOB; in dark grey), the electronic cigarette (eCIG; in purple), and the control (CON; in light green) conditions.



5. DISCUSSION

Our aim in this study was to analyse the effects of conventional and e-cigarette consumption based on basic parameters such as spirometry and arterial blood gas analysis in COPD patients. The results from spirometry demonstrated that tobacco cigarettes generate a significant detrimental effect on lung function, evident by the reduction in FEV1 and Tiffneau Index. In contrast, e-cigarettes did not produce any statistically significant effects on spirometry results. In terms of arterial blood gas analysis, PaO2, PaCO2, HCO3, and oxygen saturation were unfavourably affected by tobacco cigarettes. In contrast, e-cigarettes did not produce any statistically significant effects on the results of arterial blood gases.

Tobacco cigarette smoking undermines lung function, as serially shown in previous studies (Yates, Breen et al. 2001, Eisner, Wang et al. 2007, Metsios, Flouris et al. 2007, Flouris, Metsios et al. 2008, Flouris, Metsios et al. 2009, Flouris, Metsios et al. 2010). While chronic lung disease is normally a long-term process, we recently proposed that even brief exposures to air pollution stimulate mechanisms that contribute to its development (Flouris 2009, Flouris, Metsios et al. 2009). Acute smoking causes localised lung inflammation, platelet aggregation, reduction of the number of eosinophils, suppression of repair mechanisms and impairment of the epithelial barrier (van der Vaart, Postma et al. 2004). All these mechanisms are heavily linked with the development and/or exacerbation of chronic lung disease. In the current study, this is of paramount importance since we were assessing COPD patients. In this light, e-cigarettes appeared to be less problematic for these patients, as compared to tobacco cigarettes. Of course, this does not mean that COPD patients should freely use e-cigarettes. As we only examined the acute effects of e-cigarette use, we cannot determine the long term effects of e-cigarette use based on the present data. Indeed, spirometry may fail to detect the initial and possibly mild effects from the short-term

inhalation of e-cigarette vapour on the respiratory system while repetitive use may provoke significant changes. In a recent study where spirometry results were normal, e-cigarette use was related to an increase on flow resistance detected by impulse osscilometry. Therefore, it is likely that these oncoming pathophysiological changes may not be represented in spirometric findings yet (Vardavas, Anagnostopoulos et al. 2011). Finally, it is important to note that the present results apply to the specific e-cigarette device and liquid tested and may not describe appropriately the acute usage of other devices and/or liquids.

Based on the results of this study, it is concluded that acute e-cigarette smoking does not affect lung function (as assessed by spirometry) and arterial blood gases in COPD patients. In contrast, acute tobacco cigarette smoking undermines lung function and arterial blood gases in these patients.

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7. SUPPLEMENT

Appendix A: Ethical Review Board Approval

ΠΑΝΕΠΙΣΤΗΜΙΟ ΘΕΣΣΑΛΙΑΣ
ΤΜΗΜΑ ΕΠΙΣΤΗΜΗΣ ΦΥΣΙΚΗΣ ΑΓΩΓΗΣ ΚΑΙ ΑΘΛΗΤΙΣΜΟΥ

Εσωτερική Επιτροπή Δεοντολογίας

Τρίκαλα: 29/ 03 /2012
Αριθμ. Πρωτ.:523

Αίτηση Εξέτασης της πρότασης για διεξαγωγή Έρευνας με τίτλο: Βραχυπρόθεσμες επιπτώσεις ενεργητικού καπνίσματος συμβατικού και ηλεκτρονικού τσιγάρου στην πνευμονική λειτουργικότητα σε ασθενείς με διαγνωσμένη Χρόνια Αποφρακτική Πνευμονοπάθεια (ΧΑΠ).

Επιστημονικώς υπεύθυνος-η / επιβλέπων-ουσα: Ανδρέας Φλουρής
Ιδιότητα: Ερευνητής
Ίδρυμα: ΚΕΤΕΑΘ
Τμήμα: Ινστιτούτο Σωματικής Απόδοσης και Αποκατάστασης

Γιάννης Κουτεντάκης
Καθηγητής
ΤΕΦΑΑ
Πανεπιστήμιο Θεσσαλίας

Αθανάσιος Τζιαμούρτας
Αναπλ. Καθηγητής
ΤΕΦΑΑ
Πανεπιστήμιο Θεσσαλίας

Κύριος ερευνητής-τρια / φοιτητής-τρια: Τσάρας Θεόδωρος
Πρόγραμμα Σπουδών: ΠΜΣ «Άσκηση και Υγεία»
Ίδρυμα: ΤΕΦΑΑ
Τμήμα: Πανεπιστήμιο Θεσσαλίας

Η προτεινόμενη έρευνα θα είναι:

Ερευνητικό πρόγραμμα ☐ Μεταπτυχιακή διατριβή X Διπλωματική εργασία ☐ Ανεξάρτητη έρευνα ☐

Τηλ. επικοινωνίας: 2431 500 601
Email επικοινωνίας: andreasflouris@gmail.com

Η Εσωτερική Επιτροπή Δεοντολογίας του Τ.Ε.Φ.Α.Α., Πανεπιστημίου Θεσσαλίας μετά την υπ. Αριθμ. 1-2/22-2-2012 συνεδρίαση της εγκρίνει τη διεξαγωγή της προτεινόμενης έρευνας.

Ο Πρόεδρος της
Εσωτερικής Επιτροπής
Δεοντολογίας – ΤΕΦΑΑ

Τσιόκανος Αθανάσιος
Αναπληρωτής Καθηγητής

Appendix B: Written consent form

Έντυπο συναίνεσης δοκιμαζόμενου σε ερευνητική εργασία

Τίτλος Ερευνητικής Εργασίας: Βραχυπρόθεσμες επιπτώσεις ενεργητικού καπνίσματος συμβατικού και ηλεκτρονικού τσιγάρου στην πνευμονική λειτουργικότητα σε ασθενείς με διαγνωσμένη Χρόνια Αποφρακτική Πνευμονοπάθεια (ΧΑΠ).

Επιστημονικός Υπεύθυνος-η: Αντρέας Φλουρής, Ερευνητής, ΤΕΦΑΑ, ΠΘ, Email: aflouris@cereteth.gr, τηλ: +30 2431 500 601, +30 2431 063 190 .

Ερευνητής: Τσάρας Θεόδωρος (email: theomd@gmail.com, τηλ. 6945606100)

Σκοπός της ερευνητικής εργασίας

Σκοπός της μελέτης είναι η αξιολόγηση των βραχυπρόθεσμων επιπτώσεων στη πνευμονική λειτουργία του καπνίσματος σε ασθενείς με διαγνωσμένη ΧΑΠ μετά από κάπνισμα συμβατικού τσιγάρου (ΣΤ) και ηλεκτρονικού τσιγάρου (ΗΤ).

Διαδικασία

Οι συμμετέχοντες θα αξιολογηθούν 3 φορές στη 3η Πνευμονολογική Κλινική του ΝΝΘΑ ΣΩΤΗΡΙΑ , με μεσοδιάστημα 7 ημερών, στις 09:00 πμ. Θα έχει προηγηθεί 12ωρη αποχή από κάπνισμα, είτε ενεργητικό είτε παθητικό. Την πρώτη φορά θα ληφθεί ιστορικό της καπνιστικής τους συνήθειας.

Η ομάδα των καπνιστών τη μία ημέρα θα καπνίσει 2 ΣΤ της μάρκας τους μέσα σε διάστημα 30 λεπτών. Θα γίνει καταγραφή των ρουφηξιών που απαιτούνται για την ολοκλήρωση του καπνίσματος. Σε άλλη επίσκεψη θα καπνίσει ΗΤ, ακριβώς τον ίδιο αριθμό ρουφηξιών που απαιτήθηκαν για το κάπνισμα ΣΤ ο καθένας, μέσα σε 30 λεπτά. Σε άλλη επίσκεψη θα «καπνίσουν» ένα μη αναμμένο ΣΤ της επιλογής τους, πάλι τον ίδιο αριθμό ρουφηξιών σε 30 λεπτά (κατάσταση ελέγχου). Θα πραγματοποιηθούν κλινικές και

εργαστηριακές μετρήσεις αμέσως πριν το κάπνισμα, αμέσως μετά τη λήξη του καπνίσματος, και 1 ώρα μετά τη λήξη του καπνίσματος.

Κίνδυνοι και ενοχλήσεις

Το δείγμα αίματος θα ληφθεί από τη βραχίονιο φλέβα. Δεν υπάρχει κανένας κίνδυνος τραυματισμού κατά τη διάρκεια των δοκιμασιών. Παρ' όλα αυτά υπάρχει πρόβλεψη πρώτων βοηθειών και εκπαιδευμένο προσωπικό για κάθε ενδεχόμενο.

Προσδοκώμενες ωφέλειες

Με την συμμετοχή σας θα λάβετε πολλές πληροφορίες για το λειτουργικό σας προφίλ. Η διερεύνηση των επιδράσεων του καπνίσματος με ΗΤ ίσως αποτελέσει τη βάση για την χρήση του ως συμπληρωματικό μέσο διακοπής του καπνίσματος προς όφελος των εξαρτημένων ατόμων αλλά και του κοινωνικού συνόλου.

Δημοσίευση δεδομένων – αποτελεσμάτων

Η συμμετοχή σας στην έρευνα συνεπάγεται ότι συμφωνείτε με την μελλοντική δημοσίευση των αποτελεσμάτων της, με την προϋπόθεση ότι οι πληροφορίες θα είναι ανώνυμες και δε θα αποκαλυφθούν τα ονόματα των συμμετεχόντων. Τα δεδομένα που θα συγκεντρωθούν θα κωδικοποιηθούν με αριθμό, ώστε το όνομα σας δε θα φαίνεται πουθενά.

Πληροφορίες

Μη διστάσετε να κάνετε ερωτήσεις γύρω από το σκοπό ή την διαδικασία της εργασίας. Αν έχετε οποιαδήποτε αμφιβολία ή ερώτηση ζητήστε μας να σας δώσουμε διευκρινίσεις.

Ελευθερία συναίνεσης

Η συμμετοχή σας στην εργασία είναι εθελοντική. Είστε ελεύθερος-η να μην συναινέσετε ή να διακόψετε τη συμμετοχή σας όποτε το επιθυμείτε.

Δήλωση συναίνεσης

Διάβασα το έντυπο αυτό και κατανοώ τις διαδικασίες που θα ακολουθήσω. Συναινώ να συμμετάσχω στην ερευνητική εργασία.

Ημερομηνία: __/__/__

Ονοματεπώνυμο και υπογραφή συμμετέχοντος

Υπογραφή ερευνητή

Appendix C: Υπεύθυνη δήλωση πνευματικών δικαιωμάτων

Υπεύθυνη Δήλωση

Ο κάτωθι υπογεγραμμένος ΤΣΑΡΑΣ ΘΕΟΔΩΡΟΣ, μεταπτυχιακός φοιτητής του τμήματος ΤΕΦΑΑ του προγράμματος ΑΣΚΗΣΗ ΚΑΙ ΥΓΕΙΑ δηλώνω υπεύθυνα ότι αποδέχομαι τους παρακάτω όρους που αφορούν

(α) στα πνευματικά δικαιώματα της Μεταπτυχιακής Διπλωματικής Εργασίας (ΜΔΕ)/ Διδακτορικής διατριβής μου μου με τίτλο: *Βραχυπρόθεσμες επιπτώσεις ενεργητικού καπνίσματος συμβατικού και ηλεκτρονικού τσιγάρου στην πνευμονική λειτουργικότητα σε ασθενείς με διαγνωσμένη Χρόνια Αποφρακτική Πνευμονοπάθεια (ΧΑΠ)*.

(β) στη διαχείριση των ερευνητικών δεδομένων που θα συλλέξω στην πορεία εκπόνησής της:

1. Τα πνευματικά δικαιώματα του τόμου της μεταπτυχιακής ή διδακτορικής διατριβής που θα προκύψει θα ανήκουν σε μένα. Θα ακολουθήσω τις οδηγίες συγγραφής, εκτύπωσης και κατάθεσης αντιτύπων της διατριβής στα ανάλογα αποθετήρια (σε έντυπη ή/και σε ηλεκτρονική μορφή).

2. Η διαχείριση των δεδομένων της διατριβής ανήκει από κοινού σε εμένα και στον κύριο επιβλέποντα καθηγητή.

3. Οποιαδήποτε επιστημονική δημοσίευση ή ανακοίνωση (αναρτημένη ή προφορική), ή αναφορά που προέρχεται από το υλικό/δεδομένα της εργασίας αυτής θα γίνεται με συγγραφείς εμένα τον ίδιο, τον κύριο επιβλέποντα ή/και άλλους ερευνητές (πχ μέλη της τριμελούς συμβουλευτικής επιτροπής, συνεργάτες κλπ), ανάλογα με τη συμβολή τους στην έρευνα και στη συγγραφή των ερευνητικών εργασιών.

4. Η σειρά των ονομάτων στις επιστημονικές δημοσιεύσεις ή επιστημονικές ανακοινώσεις θα αποφασίζεται από κοινού από εμένα και τον κύριο επιβλέποντα της εργασίας, πριν αρχίσει η εκπόνησή της. Η απόφαση αυτή θα πιστοποιηθεί εγγράφως μεταξύ εμού και του κύριου επιβλέποντος.

Τέλος, δηλώνω ότι γνωρίζω τους κανόνες περί δεοντολογίας και περί λογοκλοπής και πνευματικής ιδιοκτησίας και ότι θα τους τηρώ απαρέγκλιτα καθ' όλη τη διάρκεια της φοίτησης και κάλυψης των εκπαιδευτικών υποχρεώσεων μου που προκύπτουν από το ΠΜΣ/τμήμα και καθ' όλη τη διάρκεια των διαδικασιών δημοσίευσης που θα προκύψουν μετά την ολοκλήρωση των σπουδών μου.

[- ημερομηνία –]

Ο δηλών

ΤΣΑΡΑΣ ΘΕΟΔΩΡΟΣ